

Docket No.: 19240.596US1
(PATENT)



IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant: Andrew R. Marks et al. Confirmation No.: 7653
Application No.: 10/809,089 Art Unit: 1614
Filed: March 25, 2004 Examiner: Not Yet Assigned
Title: NOVEL ANTI-ARRHYTHMIC AND HEART FAILURE DRUGS THAT
TARGET THE LEAK IN THE RYANODINE RECEPTOR (RyR2)
AND USES THEREOF

Mail Stop Amendment
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT (IDS)

Dear Sir:

Pursuant to the duty of disclosure under 37 C.F.R. §§ 1.56, 1.97 and 1.98, applicants bring to the attention of the Examiner the documents listed on the attached Form PTO SB-08. Copies of the documents listed are not submitted herewith. These documents were previously cited by or submitted to the United States Patent and Trademark Office in U.S. Patent Application No. 10/288,606, filed November 5, 2002 and is relied upon in this application for an earlier filing date under 35 U.S.C. 120.

Applicants also hereby list the following U.S. patents/patent applications that are related to this application:

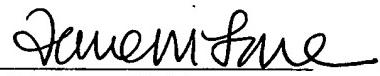
- U.S. Patent No. 6,489,125, issued December 3, 2002
- U.S. Patent Application No. 10/288,606, filed November 5, 2002
- U.S. Patent Application No. 10/608,723, filed June 26, 2003
- U.S. Patent Application No. 10/680,988, filed October 7, 2003
- U.S. Patent Application No. 10/763,498, filed January 22, 2004 (Abandoned)
- U.S. Patent Application No. 11/088,123, filed March 23, 2005
- U.S. Patent Application No. 11/088,058, filed March 23, 2005
- U.S. Provisional Application No. 60/452,644, filed March 7, 2003 (Expired)
- U.S. Patent Application No. 10/794,218, filed March 5, 2004
- U.S. Provisional Application No. 60/636,959, filed December 16, 2004 (Expired)
- U.S. Patent Application No. 11/212,309, filed August 25, 2005
- U.S. Patent Application No. 11/305,528, filed December 16, 2005

U.S. Patent Application No. 11/212,413, filed August 25, 2005
U.S. Patent Application No. 11/506,285, filed August 17, 2006

This Information Disclosure Statement is being filed prior to the mailing date of a first Office Action on the merits. No fee is required. Applicants request that the Examiner initial and return a copy of the enclosed Form PTO SB-08 with the next communication.

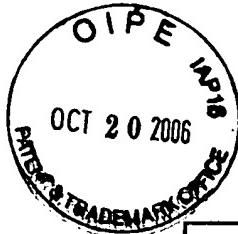
Respectfully submitted,

Dated: 10/20/06



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PTO/SB/08A/B (09-06)

Approved for use through 03/31/2007. OMB 0651-0031

U.S. Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE

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Substitute for form 1449/PTO

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(Use as many sheets as necessary)

				<i>Complete if Known</i>	
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				First Named Inventor	Andrew R. Marks
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				Examiner Name	Not Yet Assigned
Sheet	1	of	12	Attorney Docket Number	19240.596 US1

U.S. PATENT DOCUMENTS

Examiner Initials*	Cite No. ¹	Document Number	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
		Number-Kind Code ² (if known)			
	AA*	US-10/763,498	01-22-2004	Marks et al.	
	AB*	US-20030054531-A1	03-20-2003	Gretarsdottir et al.	
	AC*	US-20030134331-A1	07-17-2003	Andrew Marks	
	AD*	US-20040048780-A1	03-11-2004	Andrew Marks	
	AE*	US-20040082653-A1	04-29-2004	Nonaka et al.	
	AF*	US-20040173802	09-09-2004	Yukimoto	
	AG*	US-20040224368-A1	11-11-2004	Marks	
	AH*	US-20040229781-A1	11-18-2004	Marks et al.	
	AI*	US-20050215540-A1	09-29-2005	Marks et al.	
	AJ*	US-20060100195-A1	05-11-2006	Maruyama et al.	
	AK*	US-3,367,930-A	02-06-1968	Schmutz et al.	
	AL*	US-4,990,707	02-05-1991	Mais et al.	
	AM*	US-5,075,293	12-24-1991	Reifsneider et al.	
	AN*	US-5,180,720	01-19-1993	Husa et al.	
	AO*	US-5,182,272	01-26-1993	Hallinan et al.	
	AP*	US-5,221,681	06-22-1993	Kabbe et al.	
	AQ*	US-5,304,644	04-19-1994	Husa et al.	
	AR*	US-5,324,722	06-28-1994	Hagen et al.	
	AS*	US-5,354,747	10-11-1994	Hansen, Jr. et al.	
	AT*	US-5,416,066	05-16-1995	Kaneko et al.	
	AU*	US-5,449,675	09-12-1995	Chandrasekaran et al.	
	AV*	US-5,580,866	12-03-1996	Housley et al.	
	AW*	US-5,723,458	03-03-1998	Brieaddy et al.	
	AX*	US-5,817,652	10-06-1998	Lawrence E. Brieaddy	
	AY*	US-5,859,240	01-12-1999	Brieaddy	
	AZ*	US-5,910,494	06-08-1999	Brieaddy	
	AA1*	US-6,489,125	12-03-2002	Marks et al.	

FOREIGN PATENT DOCUMENTS

Examiner Initials*	Cite No. ¹	Foreign Patent Document	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	T ⁶
		Country Code ³ -Number ⁴ -Kind Code ⁵ (if known)				
BA	EP-1447096		08-18-2004	Ono Pharmaceutical Co		
BB	EP-1439221-A1		07-21-2004	F. Hoffmann-La Roche AG		
BC	EP-1369129		12-10-2003	Ono Pharmaceutical Co		
BD	FR-2709753		03-17-1995	Hoechst Lab		
BE	JP-05/271208		10-19-1993	Kirin Brewery Co Ltd.		
BF	JP-3093419		04-18-1991	Mitsubishi Cable Ind Ltd.		
BG	JP-11199574		07-27-1999	Ube Ind Ltd.		
BH	WO-03/034980		05-01-2003	New River Pharmaceuticals Inc.		
BI	WO-02/014246		02-21-2002	Bayer Aktiengesellschaft		
BJ	WO-04/042389-A2		05-21-2004	Bayer Healthcare AG		

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Sheet	2	of	12	Attorney Docket Number	19240.596 US1

	BK	WO-97/03986	02-06-1997	Yoshitomi Pharmaceutical Industries, Ltd.	
	BL	WO-02/051838	07-04-2002	Actelion Pharmaceuticals Ltd.	
	BM	WO-96/08228	03-21-1996	Zambon Spa et al.	
	BN	WO-2004/023030	03-18-2004	Nippon Chemi-con Corporation	
	BO	WO-02/014245	02-21-2002	Bayer Aktiengesellschaft	
	BP	WO-02/051232	07-04-2002	Actelion Pharmaceuticals Ltd.	
	BQ	WO-98/05657	02-12-1998	Knoll Aktiengesellschaft	
	BR	WO-94/11360	05-26-1994	Boots Co Plc et al.	
	BS	WO-92/19617	11-12-1992	Searle & Co	
	BT	WO-02/053548	07-11-2002	Banyu Pharmaceutical Co. Ltd.	
	BU	WO-97/17344	05-15-1997	Astra Ab et al.	
	BV	WO-03/043655	05-30-2003	Ono Pharmaceutical Co., Ltd.	
	BW	WO-01/47510	07-05-2001	Glaxo Group Limited et al.	
	BX	WO-02/08211	01-31-2002	G.D. Searle, LLC.	
	BY	WO-93/13082	11-27-1992	G.D. Searle & Co.	
	BZ	WO-04/022057	03-18-2004	Aventis Pharma Deutschland GMBH	
	BA1	WO-99/32115	07-01-1999	The University of the West Indies	
	BB1	WO-02/072145	09-19-2002	Ono Pharmaceutical Co, Ltd.	
	BC1	WO-99/26921	06-03-1999	Merck & Co Inc et al.	
	BD1	WO-94/29286	12-22-1994	Searle & Co et al.	
	BE1	WO-01/00185	01-04-2001	Knoll Aktiengesellschaft	

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. * CITE NO.: Those application(s) which are marked with an single asterisk (*) next to the Cite No. are not supplied (under 37 CFR 1.98(a)(2)(iii)) because that application was filed after June 30, 2003 or is available in the IFW. ¹ Applicant's unique citation designation number (optional). ² See Kinds Codes of USPTO Patent Documents at www.uspto.gov or MPEP 901.04. ³ Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). ⁴ For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. ⁵ Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible. ⁶ Applicant is to place a check mark here if English language Translation is attached.

NON PATENT LITERATURE DOCUMENTS			
Examiner Initials	Cite No. ¹	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T ²
	CA	"CIBIS-II, The Cardiac Insufficiency Bisoprolol Study II (CIBIS-II): A Randomized Trial." The Lancet, Vol. 353, pp. 9-13, (1999)	
	CB	Ahern et al., "Intramembrane Charge Movements and Excitation-Contraction Coupling Expressed by Two-Domain Fragments of the Ca2+ Channel." Proc Natl Acad Sci USA, Vol. 98, No. 12, pp. 6935-6940. (2001).	
	CC	Ahern et al., "Subconductance States in Single-Channel Activity of Skeletal Muscle Ryanodine Receptors After Removal of FKBP12." Biophys J, Vol. 72, pp. 146-162. (1997).	
	CD	Ahmed, G.U. et al., "Changes in Ca(2+) Cycling Proteins Underlie Cardiac Action Potential Prolongation in a Pressure-Overloaded Guinea Pig Model with Cardiac Hypertrophy and	

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		Failure." Circ. Res., Vol. 86, No. 5, pp. 558-570. (2000).	
	CE	Baille, et al., "beta-Arrestin-mediated PDE4 cAMP phosphodiesterase recruitment regulates beta-adrenoceptor switching from Gs to Gi," Proc. Natl. Acad. Sci. USA 100, 940-945 (2003).	
	CF	Barnes, P.J., "Theophylline: new perspectives for an old drug," Am. J. Respir. Crit. Care Med. 167, 813-8 (2003).	
	CG	Basso, C. et al., "Arrhythmogenic Right Ventricular Cardiomyopathy Causing Sudden Cardiac Death in Boxer Dogs: A New Animal Model of Human Disease." Circulation, Vol. 109, No. 9, pp. 1180-1185. (2004).	
	CH	Bennett et al., "Synthesis of 2-methoxydibenzo [b,f](1,4)-thiazepin-11 (10H)-one 5,5-dioxide." Organic Preparations and Procedures International, Vol. 6, No. 6, pp. 287-293. (1974).	
	CI	Bezprozvanny, I. et al. "Bell-shaped Calcium Response Curves of Ins (1,4,5) P3- and Calcium-gated Channels from Endoplasmic Reticulum of Cerebellum." Nature, Vol. 351, pp. 751-754. (1991).	
	CJ	Bittar, et al., "The arrhythmogeneity of theophylline. A multivariate analysis of clinical determinants," Chest 99, 1415-1420 (1991).	
	CK	Bohm, M. et al. "cAMP Concentrations, cAMP Dependent Protein Kinase Activity, and Phospholamban in Non-Failing and Failing Myocardium." Cardivasc. Res., Vol. 28, No. 11, pp. 1713-1719. (1994).	
	CL	Bolger, et al., "Characterization of five different proteins produced by alternatively spliced mRNAs from the human cAMP-specific phosphodiesterase PDE4D gene," Biochem. J. 328 (Pt 2), 539-48 (1997).	
	CM	Boyden et al., "2APB- and JTV519 (K201) - Sensitive Micro Ca ²⁺ Waves in Arrhythmogenic Purkinje Cells that Survive in Infarcted Canine Heart." Heart Rhythm, Vol. 1, pp. 218-226. (2004).	
	CN	Bristow et al., "Carvedilol Produces Dose-Related Improvements in left Ventricular Function and Survival in Subjects with Chronic Heart Failure." Circulation, Vol. 94, pp. 2807-2816. (1996).	
	CO	Bristow, et al., "Beta 1- and beta 2-adrenergic-receptor subpopulations in nonfailing and failing human ventricular myocardium: coupling of both receptor subtypes to muscle contraction and selective beta 1-receptor down-regulation in heart failure," Circ. Res. 59, 297-309 (1986).	
	CP	Bristow, Michael R. et al. "B-Adrenergic Neuroeffector Abnormalities in the Failing Human Heart are Produced by Local Rather Than Systemic Mechanisms." J. Clin. Invest., Vol. 89, pp. 803-815 (March 1982).	
	CQ	Callaway, C. et al., "Localization of the High and Low Affinity [³ H] Ryanodine Binding Sites on the Skeletal Muscle Ca ²⁺ Release Channel." The Journal of Biological Chemistry, Vol. 269, No. 22, pp. 15876-15884. (1994).	
	CR	Carlisle Michel, et al., "PKA-phosphorylation of PDE4D3 facilitates recruitment of the mAKAP signaling complex," Biochem. J. 381, 587-592 (2004).	
	CS	Catsoulacos, "Synthesis of Substituted Dihydrobenzothiazepines and Related Compounds." J Heterocyclic Chemistry, Vol. 7, No. 2: pp. 409-411. (1970).	
	CT	Cerrone, M. et al., "Bidirectional Ventricular Tachycardia and Fibrillation Elicited in a Knock-in Mouse Model Carrier of a Mutation in the Cardiac Ryanodine Receptor." Circ. Res., Vol. 96, No. 10, e77-82. (2005).	
	CU	Cheng, H. et al., "Amplitude Distribution of Calcium Sparks in Confocal Images: Theory and Studies with an Automatic Detection Method." Biophys J., Vol. 76, pp. 606-617. (1999).	
	CV	Cohn, J.N. et al. "Plasma Norepinephrine as a Guide to Prognosis in Patients with Chronic Congestive Heart Failure." N. Eng. J. Med., Vol. 311, No. 13, pp. 819-823 (1984).	

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Sheet	4	of	12	Attorney Docket Number	19240.596 US1

CW	Conti, et al., "Cyclic AMP-specific PDE4 phosphodiesterases as critical components of cyclic AMP signaling," J. Biol. Chem. 278, 5493-6 (2003).	
CX	Dietz et al., "Epinephrine Regulation of Skeletal Muscle Glycogen Metabolism :Studies Utilizing the Perfused Rat Hindlimb Preparation." J. Biol. Chem., Vol. 255, No. 6, pp. 2301-2307. (1980).	
CY	Dodge K.L., et al. "mAKAP Assembles a Protein Kinase A/PDE4 Phosphodiesterase cAMP Signaling Module." EMBO J. Vol. 20, No. 8, pp. 1921-1930. (2001).	
CZ	Doi et al., "Propranolol prevents the Development of Heart Failure by Restoring FKBP12.60-Mediated Stabilization of Ryanodine Receptor." Circulation Vol. 105, pp. 1374-1379. (2002).	
CA1	Drexler et al. "Contrasting Peripheral Short-Term and Long-Term Effects of Coverting Enzyme Inhibition in Patients with Congestive Heart Failure. A Double-Blind, Placebo-Controlled Trial." Circulation, Vol. 79, pp. 491-502. (1989).	
CB1	Exhibit I: Structures	
CC1	Feldman, et al., "Deficient production of cyclic AMP: pharmacologic evidence of an important cause of contractile dysfunction in patients with end-stage heart failure," Circulation 75, 331-9 (1987).	
CD1	Fisher, J.D. et al. "Familial Polymorphic Ventricular Arrhythmias: A Quarter Century of Successful Medical Treatment Based on Serial Exercise-Pharmacologic Testing." J. Am. Coll. Cardiol., Vol. 34, No. 7, pp. 2015-2022. (1999).	
CE1	Fodor et al. "New Convenient Synthesis of 1,4-benzothiazepines." Tetrahedron Letters, Vol. 36, No. 5, pp. 753-756. (1995).	
CF1	Fox, P.R., "Spontaneously Occurring Arrhythmogenic Right Ventricular Cardiomyopathy in the Domestic Cat: A New Animal Model Similar to the Human Disease." Circulation, Vol. 102, No. 15, pp. 1863-1870. (2000).	
CG1	Franzen, P. et al. "Cloning of a TGF β Type I Receptor That Forms a Heteromeric Complex with the TGF beta type II receptor." Cell, Vol. 75, pp. 681-692. (1993).	
CH1	Franzini-Armstrong et al., "Alternate Disposition of Tetradis in Peripheral Couplings of Skeletal Muscle." Journal of Muscle Research & Cell Motility." Vol. 16, pp. 319-324. (1995).	
CI1	Fraser, I.D. et al. "Modulation of Ion Channels: a "current" view of AKAPs." Neuron, Vol. 23, pp. 423-426. (1999).	
CJ1	Frazier, O.H. et al. "First Use of an Untethered, Vented Electric Left Ventricular Assist Device for Long-Term Support." Circulation, Vol. 89, pp. 2908-2914. (1994).	
CK1	Gaburjakova, M. et al. "FKBP12 Binding Modulates Ryanodine Receptor Channel Gating." J. Biol. Chem., Vol. 276, No.20, pp. 16931-16935. (2001).	
CL1	Giembycz, M.A., "Development status of second generation PDE4 inhibitors for asthma and COPD: the story so far," Monaldi, Arch. Chest Dis. 57, 48-64 (2002).	
CM1	Go, Loewe O. et al., "Differential Regulation of Two Types of Intracellular Calcium Release Channels during End-Stage Heart Failure." J. Clin. Invest., Vol. 95, pp. 888-894. (February 1995)	
CN1	Goette et al. "Electrical Remodeling in Atrial Fibrillation: Time Course and Mechanisms." Circulation, Vol. 94, pp. 2968-2974. (1996).	
CO1	Gong, et al., "Persistent improvement in synaptic and cognitive functions in an Alzheimer mouse model after rolipram treatment," J. Clin. Invest. 114, 1624-1634 (2004)	
CP1	Gonzalez et al. "Involvement of Multiple Intracellular Release Channels in Calcium Sparks of Skeletal Muscle." Proc. Natl Acad Sci USA, Vol. 97, No. 8, pp. 4380-4385. (2000).	
CQ1	Gretarsdottir, et al., "The gene encoding phosphodiesterase 4D confers risk of ischemic stroke," Nat. Genet. 35, 131-8 (2003).	

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	CR1	Gullestad et al., "Effect of Metoprolol CR/XL on Exercise Tolerance in Chronic Heart Failure - a Substudy to the MERIT-HF Trial," Eur. J. Heart Fail, Vol. 3, pp. 463-468. (2001).	
	CS1	Hachida et al. "Protective effect of JTV519 on Prolonged Myocardial Preservation." Transplant Proc., Vol. 31, pp. 1094. (1999).	
	CT1	Hachida et al. "Significant Effect of 1,4-Benzothiazepine Derivative (K2) in Improving Myocardial Preservation." Transplantation Proceedings, Vol. 29, pp. 1346-1348. (1997).	
	CU1	Hachida, et al., "Protective Effect of JTV519 (K201), a New 1, 4 - Benzothiazepine Derivative, on Prolonged Myocardia Preservation." Transplantation Proceedings, Vol. 31, pp. 996-1000. (1999).	
	CV1	Hachida, M. et al. "Protective Effect of JTV-519, a new 1, 4-Benzothiazepine Derivative, on Prolonged Myocardial Preservation." J. Card. Surg., Vol. 14, pp. 187-193. (1999).	
	CW1	Harnick, D.J. et al. "The Human Type 1 Inositol 1,4,5-trisphosphate receptor from T Lymphocytes: Structure, Localization, and Tyrosine Phosphorylation." J. Biol. Chem., Vol. 270, No. 6, pp. 2833-2840. (1995.)	
	CX1	Harrington, D. et al. "Mechanisms of Exercise Intolerance in Congestive Heart Failure." Current Opinion in Cardiology, Vol. 12, No. 3, pp. 224-32. (1997).	
	CY1	Hasenfuss et al., "Treatment of Heart Failure Through Stabilization of the Cardiac Ryanodine Receptor." Circulation, Vol. 107, pp. 378-380. (2003).	
	CZ1	Houslay, et al., "PDE4 cAMP phosphodiesterases: modular enzymes that orchestrate signaling cross-talk, desensitization and compartmentalization," Biochem. J. 370, 1-8 (2003).	
	CA2	Huse, M. et al. "Crystal Structure of the Cytoplasmic Domain of the Type 1 TGF β Receptor in Complex With FKBP12." Cell, Vol. 96, pp. 425-436. (1999).	
	CB2	Inagaki et al. "Anti-ischemic Effect of a Novel Cardioprotective Agent, JTV 519, is mediated through Specific Activation of 8-Isoform of Protein Kinase C in Rat Ventricular Myocardium." Circulation, Vol. 101, pp. 797-804. (2000).	
	CC2	Inagaki et al. "The Cardioprotective Effects of a new 1,4-benzothiazepine Derivative, JTV 519, on ischemia/reperfusion-induced Ca $^{2+}$ Overload in Isolated Rat Hearts." Cardiovasc Drugs Ther., Vol. 14, pp. 489-495. (2000).	
	CD2	International Search Report and Written Opinion from PCT/US04/20474, August 30, 2005.	
	CE2	International Search Report and Written Opinion from PCT/US04/32550, October 18, 2005.	
	CF2	International Search Report and Written Opinion from PCT/US05/009495, March 14, 2006.	
	CG2	International Search Report and Written Opinion from PCT/US05/10055, October 27, 2005.	
	CH2	International Search Report and Written Opinion from PCT/US05/45914, August 31, 2006	
	CI2	Ito et al. "JTV-519, a Novel Cardioprotective Agent, Improves the Contractile Recovery after Ischaemia Reperfusion in Coronary Perfused Guinea Pig Ventricular Muscles." Br. J. Pharmacol., Vol. 130, No. 4, pp. 767-776. (2000).	
	CJ2	Jayaraman, T. et al. "Regulation of the Inositol 1,4,5-Trisphosphate Receptor By Tyrosine Phosphorylation." Science, Vol. 272, pp. 1492-1494. (1996.)	
	CK2	Jiang et al., "Abnormal Ca $^{2+}$ Release, but Normal Ryanodine Receptors, in Canine and Human Heart Failure." Circulation Research, Vol. 91, pp. 1015-1022. (November 29, 2002).	
	CL2	Jiang, D. et al. "Enhanced Basal Activity of a Cardiac Ca $^{2+}$ Release Channel (Ryanodine Receptor) Mutant Associated with Ventricular Tachycardia and Sudden Death." Circ. Res., Vol. 91, pp. 218-225. (2002).	
	CM2	Jin, S.L.C. et al.: "Impaired growth and fertility of cAMP-specific phosphodiesterase PDE4D-deficient mice," PNAS, October 12, 1999, vol. 96, no. 21, 11998-12003.	
	CN2	Kaneko et al., "Crystal Structure of Annexin V with Its Ligand K-201 as a Calcium Channel Activity Inhibitor." Journal of Molecular Biology, Vol. 274, pp. 16-20. (1997).	

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	CO2	Kaneko et al., "Inhibition of Annexin V-dependent Ca2 Movement in Large Unilamellar Vesicles by K201, a New." <i>Biochimica et Biophysica Acta</i> , Vol. 1330, pp. 1-7. (1997).	
	CP2	Kaneko, N. "New 1,4-benzothiazepine Derivative, K201, Demonstrates Cardio-Protective Effects Against Sudden Cardiac Cell Death and Intracellular Calcium Blocking Action." <i>Drug Dev. Res.</i> , Vol. 33, pp. 429-438 (1994).	
	CQ2	Kapiloff, M.S. et al. "mAKAP:an A-kinase Anchoring Protein Targeted to the Nuclear Membrane of Differentiated Myocytes." <i>J. Cell Sci.</i> , Vol. 112, pp. 2725-2736. (1999).	
	CR2	Kapiloff, M.S. et al.: "mAKAP and the ryanodine receptor are part of a multi-component signaling complex on the cardiomyocyte nuclear envelope," <i>Journal of Cell Science</i> , 114, 3167-3176 (2001).	
	CS2	Katritzky, et al., "1H and 13C NMR study of tetrahydro-1, 4-benzothiazepine conformations," <i>J. Chem. Soc.</i> 5, 1816-1822 (2002).	
	CT2	Katritzky, et al., "Convenient syntheses of 2, 3, 4, 5-tetrahydro-1, 4-benzothiazepines, -1, 4-benzoxazepines and -1, 4-benzodiazepines, <i>J. Chem. Soc.</i> 11, 592-598 (2002).	
	CU2	Katz et al., "Lactate Turnover at Rest and During Submaximal Exercise in Patients with Heart Failure." <i>J. Appl. Physiol.</i> , Vol. 75, No. 5, pp. 1974-1979. (1993).	
	CV2	Kawabata et al. "A Novel Cardioprotective Agent, JTV-519, is abolished by Nitric Oxide Synthase Inhibitor on Myocardial Metabolism in Ischemia-Reperfused Rabbit Hearts." <i>Hypertens Res.</i> , Vol. 25, pp. 303-309. (2001).	
	CW2	Kawabata et al. "Effect of a Novel Cardioprotective Agent, JTV-519, on Metabolism, Contraction and Relaxation in the Ischemia-Reperfused Rabbit Heart." <i>Jpn Circ. J.</i> , Vol. 64, pp. 772-776. (2000)	
	CX2	Kimura, J. et al. "Effects of a Novel Cardioprotective Drug, JTV-519 on Membrane Currents of Guinea Pig Ventricular Myocytes." <i>Jpn. J. Pharmacol.</i> , Vol. 79, pp. 275-281. (1999).	
	CY2	Kirchhefer, U. et al. "Activity of cAMP-dependent Protein Kinase and Ca2+/calmodulin-dependent Protein Kinase in Failing and Nonfailing Human Hearts." <i>Cardiovasc. Res.</i> , Vol. 42, pp. 254-261 (1999).	
	CZ2	Kiryama et al. "Effects of JTV-519, a Novel Anti-Ischaemic Drug, on the Delayed Rectifier K+ Current in Guinea-Pig Ventricular Myocytes." <i>Naunyn Schmiedebergs Arch Pharmacol.</i> Vol. 361, No. 6, pp. 646-653. (2000).	
	CA3	Kirsch et al., "Spark and Ember-Like Elementary Ca2+ Release Events in Skinned Fibre of Adult Mammalian Skeletal Muscle." <i>J. Physiol.</i> , Vol. 537, No. 2, pp. 379-389. (2001).	
	CB3	Kiryu, K. et al. "Pathologic and Electrocardiographic Findings in Sudden Cardiac Death in Racehorses." <i>J. Vet. Med. Sci.</i> , Vol. 61, No. 8, pp. 921-928. (1999).	
	CC3	Kittleson, M.D. et al., "Familial Hypertrophic Cardiomyopathy in Maine Coon Cats: An Animal Model of Human Disease." <i>Circulation</i> , Vol. 99, No. 24, pp. 3172-3180. (1999).	
	CD3	Klein et al., "Voltage Dependence of the Pattern and Frequency of Discrete Ca2+ Release Events After Brief Repriming in Frog Skeletal Muscle." <i>Proc. Natl. Acad. Sci. USA</i> , Vol. 94, pp. 11061-11066. (1997).	
	CE3	Kukin, M.L. et al. "Prospective, Randomized Comparison of Effect of Long-Term Treatment with Metoprolol or Carvedilol on Symptoms, Exercise, Ejection Fraction, and Oxidative Stress in Heart Failure." <i>Circulation</i> , Vol. 99, pp. 2645-2651. (1999).	
	CF3	Lacampagne, A. et al., "Modulation of the Frequency of Spontaneous Sarcoplasmic Reticulum Ca2+ Release Events (Ca2+ Sparks) by Myoplasmic (Mg2+) Frog Skeletal Muscle." <i>J. Gen. Physiol.</i> 111, pp. 207-224. (1998).	
	CG3	Laflamme, M.A. et al. "Gs and Adenylyl Cyclase in Transverse Tubules of Heart: Implications for cAMP-dependent signaling." <i>Am. J. Phys.</i> , Vol. 277, pp. H1841-H1848. (1999).	

Examiner Signature	Date Considered
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Substitute for form 1449/PTO				Complete if Known	
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Sheet	7	of	12	Attorney Docket Number	19240.596 US1

	CH3	Lai, F.A., et al., "The Ryanodine Receptor-Ca ²⁺ Release Channel Complex of Skeletal Muscle Sarcoplasmic Reticulum. Evidence for a Cooperatively Coupled, Negatively Charged Homotetramer." J. Biol. Chem., Vol. 264, No. 28, pp. 16776-16785. (1989).	
	CI3	Lamb et al., "Effects of FK506 and Rapamycin on Excitation-Contraction Coupling in Skeletal Muscle Fibres of the Rat." J Phys, Vol. 494, No.2, pp. 569-576. (1996).	
	CJ3	Lauffenburger et al. , "Receptors." Oxford University Press, Chapter 2, pp. 9-12. (1996).	
	CK3	Laver et al., "Inactivation of Ca ²⁺ Release Channels (Ryanodine Receptors RyR1 and RyR2) with Rapid Steps in [Ca ²⁺] and Voltage." Biophys J., Vol. 74, pp. 2352-2364. (1998).	
	CL3	Lehnart et al. "Cardiac Ryanodine Receptor Function and Regulation in Heart Disease." Ann NY Acad Sci., Vol. 1015, pp. 144-159. (2004).	
	CM3	Lehnart et al. "Defective Ryanodine Receptor Interdomain Interactions May Contribute to Intracellular Ca ²⁺ Leak: A Novel Therapeutic Target in Heart Failure." Circulation, Vol. 111, No. 25, pp. 3342-3346. (2005).	
	CN3	Lehnart et al., "Phosphodiesterase 4D Deficiency in the Ryanodine-Receptor Complex Promotes Heart Failure and Arrhythmias." Cell, Vol. 123, No. 1, pp. 25-35. (October 7, 2005).	
	CO3	Lehnart et al., "Sudden Death in Familial Polymorphic Ventricular Tachycardia Associated with Calcium Release Channel (Ryanodine Receptor) Leak." Circulation, Vol. 109, pp. 3208-3214. (2004).	
	CP3	Levin, H.R. et al. "Reversal of Chronic Ventricular Dilation in Patients with End-Stage Cardiomyopathy by Prolonged Mechanical Unloading." Circulation, Vol. 91, pp. 2717-2720. (1995).	
	CQ3	Lisy et al., "New Cardioprotective Agent K201 is Natriuretic and Glomerular Filtration Rate Enhancing." Circulation, Vol. 113, pp. 246-251. (2006).	
	CR3	Lorenz, M.C. et al. "TOR Mutations Confer Rapamycin Resistance by Preventing Interaction with FKBP12- Rapamycin." J. Biol. Chem., Vol. 270, No. 46, pp. 27531-27537. (1995).	
	CS3	Lunde et al., "Contraction and Intracellular Ca ²⁺ Handling in Isolated Skeletal Muscle of Rats with Congestive Heart Failure." Circ. Res., Vol. 88, pp. 1299-1305. (2001).	
	CT3	Lunde, et al. "Contractile Properties of in Situ Perfused Skeletal Muscles from Rats with Congestive Heart Failure." J. Physiol, Vol. 540, pp. 571-580. (2002).	
	CU3	MacDougall, L.K. et al. "Identification of the Major Protein Phosphatases in Mammalian Cardiac Muscle Which Dephosphorylate Phospholamban." Eur. J. Biochem., Vol. 196, pp. 725-734. (1991).	
	CV3	MacFarlane et al. "Cellular Basis for Contractile Dysfunction in the Diaphragm from a Rabbit Infarct Model of Heart Failure." Am. J. Physiol. Cell Physiol., Vol. 278, pp. C739-C746. (2000).	
	CW3	Mancini et al., "Contribution of a Skeletal Muscle Atrophy to Exercise Intolerance and Altered Muscle Metabolism in Heart Failure." Circulation, Vol. 85, pp. 1364-1373 (1992).	
	CX3	Marks et al. "Clinical Implications of Cardiac Ryanodine Receptor/Calcium Release Channel Mutation Linked to Sudden Cardiac Death." Circulation, Vol. 106, pg. 8-10. (July 2, 2002).	
	CY3	Marks et al. "Involvement of the Cardiac Ryanodine Receptor/Calcium Release Channel in Catecholaminergic Polymorphic Ventricular Tachycardia." J. Cell. Physiol., Vol. 190, pp. 1-6. (January 2002).	
	CZ3	Marks et al. "Ryanodine Receptors, FKBP12, and Heart Failure." Frontiers in Bioscience, Vol. 7, pp. 970-977. (2002).	
	CA4	Marks et al., "A Guide for the Perplexed: Towards an Understanding of the Molecular Basis of Heart Failure." Circulation, Vol. 107, pp. 1456-1459. (2003).	
	CB4	Marks, A.R. et al. "Involvement of the Cardiac Ryanodine Receptor/Calcium Release Channel in Catecholaminergic Ventricular Tachycardia (Familial Polymorphic Ventricular Tachycardia)"	

Examiner Signature	Date Considered
--------------------	-----------------

Substitute for form 1449/PTO				<i>Complete if Known</i>	
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Sheet	8	of	12	Attorney Docket Number	19240.596 US1

	J. Cellular Physiology, Vol. 190, pp. 1-6. (2001).
CC4	Marks, Andrew. "Ryanodine Receptors/Calcium Release Channels in Heart Failure and Sudden Cardiac Death," Journal of Molecular Cell Cardiology, Vol. 33, pp. 615-624. (2001).
CD4	Marx et al. "Beta-Adrenergic Receptor Modulation of the KCNQ1/KCNE1 Potassium Channel Requires a Macromolecular Signaling Complex." Science, Vol. 295, pp. 495-499. (2002).
CE4	Marx S.O et al., "Regulation of the Ryanodine Receptor in Heart Failure." Basic Res. Cardiol., Vol. 97, Suppl. 1, pp. 1/49-1/51. (2002).
CF4	Marx, S.O. "Requirement of a Macromolecular Signaling Complex for β Adrenergic Receptor Modulation of the KCNQ1-KCNE1 Potassium Channel." Science, Vol. 295, pp. 496-499. (2002).
CG4	Marx, S.O. et al. "Phosphorylation-dependent Regulation of Ryanodine Receptors: A Novel Role for Leucine/Isoleucine Zippers." J. Cell. Biol., Vol. 153, No. 4, pp. 699-708. (2001).
CH4	Marx, Steven O. et al. "Coupled Gating Between Individual Skeletal Muscle Ca^{2+} Release Channels (Ryanodine Receptors)." Science, Vol. 281, pp. 818-821. (August 7, 1998).
CI4	Masumiya et al., "Localization of the 12.6 kDa FK506-binding Protein (FKBP12.6) Binding Site to the NH_2 - Terminal Domain of the Cardiac Ca^{2+} Release Channel. (Ryanodine Receptor)." The Journal of Biological Chemistry, Vol. 278, pp. 3786-3792. (2003).
CJ4	McCartney, S. et al. "Cloning and Characterization of A-Kinase Anchor Protein 100 (AKAP100). A Protein That Targets A-Kinase to the Sarcoplasmic Reticulum." J. Biol. Chem., Vol. 270, No. 16, pp. 9327-9333. (1995).
CK4	Meissner, G., "Ryanodine Receptor/ Ca^{2+} Release Channels and Their Regulation by Endogenous Effectors." Annu. Rev. Physiol., Vol. 56, pp. 485-508. (1994).
CL4	Merit, H.F. "Effect of Metoprolol CR/XL in Chronic Heart Failure: Metoprolol CR/XL Randomised Intervention Trial in Congestive Heart Failure (MERIT-HF)." Lancet, Vol. 353, pp. 2001-2007. (1999).
CM4	Meurs, K.M. et al., "A Cardiac Myosin Binding Protein C Mutation in the Maine Coon Cat with Familial Hypertrophic Cardiomyopathy." Hum Mol Genet, Vol. 14, No. 23, pp. 3587-3593. (2005).
CN4	Meurs, KM. "Boxer Dog Cardiomyopathy: An Update." Vet Clin North Am Small Anim Pract., Vol. 34, pp. 1235-1244. (2004).
CO4	Miller, K.B., "Manganese Alters Mitochondrial Integrity in the Hearts of Swine Marginally Deficient in Magnesium." Biofactors, Vol. 20, No. 2, pp. 85-96. (2004).
CP4	Minotti et al., "Impaired Skeletal Muscle Function in Patients with Congestive Heart Failure. Relationship to Systemic Exercise Performance." J. Clin. Invest., Vol. 88, pp. 2077-2082. (1991).
CQ4	Mitchell, G.F. et al. "Measurement of Heart Rate and Q-T Interval in the Conscious Mouse." Am. J. Physiol., Vol. 274, pp. H747-H751. (1998).
CR4	Moghadam, H.K. "Heritability of Sudden Death Syndrome and Its Associated Correlations to Ascites and Body Weight in Broilers." Br Poult Sci, Vol. 46, No. 1, pp. 54-57. (2005).
CS4	Moise, N.S., "Inherited Arrhythmias in the Dog: Potential Experimental Models of Cardiac Disease." Cardiovasc Res, Vol. 44, No. 1, pp. 37-46. (1999).
CT4	Mongillo, et al., "Fluorescence resonance energy transfer-based analysis of cAMP dynamics in live neonatal rat cardiac myocytes reveals distinct functions of compartmentalized phosphodiesterases," Cir. Res., 95, 67-75 (2004).
CU4	Morgan, J. et al. "Abnormal Intracellular Calcium Handling: A Major Cause of Systolic and Diastolic Dysfunction in Ventricular Myocardium from Patients with heart failure." Circulation, Vol. 81 (Suppl. 3), pp. III21-III32. (1990).

Examiner Signature	Date Considered
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CV4	Moschella, M.C. et al.: Inositol 1,4,5-trisphosphate Receptor Expression in Cardiac Myocytes." J. Cell. Biol., Vol. 120, No. 5, pp. 1137-1146. (1993).	
CW4	Nair, et al., "Synthesis and reactions of 1, 4-benzothiazepine derivatives," IJOCAP, 7(9), 862-5 (1969).	
CX4	Nakai, et al., "Functional Nonequality of the Cardiac and Skeletal Ryanodine Receptors," Proc. Natl. Acad. Sci. USA, Vol. 94, pp. 1019-1022, February 1997	
CY4	Nakamura, Y. et al., "Parasitic Females of Strongyloides Papillosum as a Pathogenetic Stage for Sudden Cardiac Death in Infected Lambs." J. Vet Med. Sci., Vol. 56, No. 4, pp. 723-727. (1994).	
CZ4	Nakaya et al. "Inhibitory Effects of JTV-519, a Novel Cardioprotective Drug, on Potassium Currents and Experimental Atrial Fibrillation in Guinea-Pig Hearts. British Journal of Pharmacology," Vol. 131, pp. 1363-1372. (2000).	
CA5	Neumann, J. et al. "Increased Expression of Cardiac Phosphatases in Patients with End-Stage Heart Failure." J. Mol. Cell. Cardiol., Vol. 29, pp. 265-272. (1997).	
CB5	Otsu, K. et al. "Molecular Cloning of cDNA encoding the Ca ²⁺ release channel (Ryanodine Receptor) of Rabbit Cardiac Muscle Sarcoplasmic Reticulum." J. Biol. Chem., Vol. 265, No. 23, pp. 13472-13483. (1990).	
CC5	Oyama, Mark A. et al., "Genomic Expression Patterns of Cardiac Tissues from Dogs with Dilated Cardiomyopathy." AJVR, Vol. 66, No. 7, pp. 1140-1155. (July 2005).	
CD5	Packer, et al., "Effect of oral milrinone on mortality in severe chronic heart failure. The PROMISE Study Research Group," N. Engl. J. Med. 325, 1468-75 (1991).	
CE5	Perreault et al., "Alterations in Contractility and Intracellular Ca ²⁺ Transients in Isolated Bundles of Skeletal Muscle Fibers from Rats with Chronic Heart Failure." Circ. Res., Vol. 73, No. 2, pp. 405-412. (1993).	
CF5	Perry, et al., "Targeting of cyclic AMP degradation to beta 2-adrenergic receptors by beta-arrestins," Science 298, 834-6 (2002).	
CG5	Pieske, et al., "Ca ²⁺ handling and sarcoplasmic reticulum Ca ²⁺ content in isolated failing and nonfailing human myocardium," Circ. Res. 85, 38-46 (1999).	
CH5	Pogwizd, S.M. et al. "Mechanisms Underlying Spontaneous and Induced Ventricular Arrhythmias in Patients with Idiopathic Dilated Cardiomyopathy." Circulation, Vol. 98, pp. 2404-2414. (1998).	
CI5	Pogwizd, S.M. et al. "Arrhythmogenesis and Contractile Dysfunction in Heart Failure: Roles of Sodium-Calcium Exchange, Inward Rectifier Potassium Current, and Residual Beta-Adrenergic Responsiveness." Circ. Res., Vol. 88, pp. 1159-1167. (2001).	
CJ5	Protas, L. et al., "Regional Dispersion of L-type Calcium Current in Ventricular Myocytes of German Shepherd Dogs with Lethal Cardiac Arrhythmias." Heart Rhythm, Vol. 2, Issue. 2, pp. 172-176. (2005).	
CK5	Regitz-Zagrosek, et al. "Myocardial Cyclic AMP and Norepinephrine Content in Human Heart Failure." Eur. Heart J, 15 Suppl. D: pp. 7-13. (1994).	
CL5	Reiken et al. "PKA Phosphorylation Activates the Calcium Release Channel (Ryanodine Receptor) in Skeletal Muscle: Defective Regulation in Heart Failure." J. Cell. Biol., Vol. 160, No. 6, pp. 919-928. (2003).	
CM5	Reiken et al. "Protein Kinase A Phosphorylation of the Cardiac Calcium Release Channel (Ryanodine Receptor) in Normal and Failing Hearts. Role of Phosphatases and Response to Isoproterenol." J. Biol. Chem., Vol. 278, No. 1, pp. 444-453. (2003).	
CN5	Reiken et al., "A Novel Excitation-Contraction (EC) Coupling Myopathy in Heart Failure Involving Both Cardiac and Skeletal Muscles." Circulation, Vol. 104, No. 17 Supplement, pp.	

Examiner Signature	Date Considered
--------------------	-----------------

Substitute for form 1449/PTO				<i>Complete if Known</i>	
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				Examiner Name	Not Yet Assigned
Sheet	10	of	12	Attorney Docket Number	19240.596 US1

		II.131. (October 23, 2001).	
	CO5	Reiken et al., "Defective Skeletal Muscle Calcium Release Channel Function during Heart Failure." Circulation, Vol. 106, No. 19 Supplement, pp. II-225. (2002).	
	CP5	Reiken, S. et al. "PKA Phosphorylation of the Cardiac Calcium Release Channel (Ryanodine Receptor) in Normal and Failing Hearts: Role of Phosphatases and Response to Isoproterenol." J. Biol. Chem. (2002).	
	CQ5	Reiner, G. et al., "Skeletal Muscle Sarcoplasmic Calcium Regulation and Sudden Death Syndrome in Chickens." Br Poult Sci., Vol. 36, No. 4, pp. 667-675. (1995).	
	CR5	Richter, et al., "Splice variants of the cyclic nucleotide phosphodiesterase PDE4D are differentially expressed and regulated in rat tissue," Biochem. N. 388, 803-811 (2005).	
	CS5	Rios et al., "Charge Movement and the Nature of Signal Transduction in Skeletal Muscle Excitation-Contraction Coupling." Annu Rev Physiol, Vol. 54, pp. 109-133. (1992).	
	CT5	Rios et al., "Involvement of Dihydropyridine Receptors in Excitation-Contraction Coupling in Skeletal Muscle." Nature, Vol. 325, pp. 717-720. (1987).	
	CU5	Ruehr, et al., "Targeting the protein kinase A by muscle A kinase-anchoring protein (mAKAP) regulates phosphorylation and function of the skeletal muscle ryanodine receptor," J. Biol. Chem. 278, 24831-24836 (2003).	
	CV5	Schneider et al., "Voltage Dependent Charge Movement in Skeletal Muscle: A Possible Step in Excitation-Contraction Coupling." Nature, Vol. 242, pp. 244-246. (1973).	
	CW5	Schoenmakers et al., "CHELATOR: An Improved Method for Computing Metal Ion Concentrations in Physiological Solutions." Biocomputing, Vol. 12, pp. 870-879. (1992).	
	CX5	Sen, L.Y. et al. "Inotropic and Calcium Kinetic Effects of Calcium Channel Agonist and Antagonist in Isolated Cardiac Myocytes from Cardiomyopathic Hamsters." Circ Res, Vol. 67, No. 3, pp. 599-608. (1990).	
	CY5	Sette, et al., "Phosphorylation and activation of a cAMP-specific phosphodiesterase by the cAMP-dependent protein kinase. Involvement of serine 54 in the enzyme activation," J. Biol. Chem. 271, 16526-34 (1996).	
	CZ5	Sette, et al., "The ratPDE3/lvd phosphodiesterase gene codes for multiple proteins differentially activated by cAMP-dependent protein kinase," J. Biol. Chem. 269, 18271-4 (1994).	
	CA6	Shannon, et al., "Elevated sarcoplasmic reticulum Ca ²⁺ leak in intact ventricular myocytes from rabbits in heart failure," Circ. Res. 93, 592-4 (2003).	
	CB6	Shibata, "264 W94" Current Opinion in Cardiovascular, Pulmonary, and Renal Investigational Drugs., Vol. 1, No. 2, pp. 276-278. (1999).	
	CC6	Shinohara, "A Synthesis of Mono-and Dimethoxy -1,2,3,4 - Tetrahydroisoquinolines via Pummerer Reaction: Effects of Methoxyl Groups on Intramolecular Cyclization." Chemical and Pharmaceutical Bulletin, Vol. 46, No. 6, pp. 918-927. (1998).	
	CD6	Shirokova, N. et al., "Local Calcium Release in Mammalian Skeletal Muscle." J. Physiol, Vol. 512, No. 2, pp. 377-384. (1998).	
	CE6	Shou, W. et al. "Cardiac Defects and Altered Ryanodine Receptor Function in Mice Lacking FKBP12." Nature, Vol. 391, pp. 489-492. (1998).	
	CF6	Sonneitner et al., "Gating of the Skeletal Calcium Release Channel by ATP is Inhibited by Protein Phosphatase 1 but not by Mg ²⁺ ." Cell Calcium 21, No. 4, pp. 283-290. (1997).	
	CG6	Sorensen et al., "Excercised Blood Flow and Microvascular Distensibility in Skeletal Muscle Normalize After Heart Transplantation." Clin. Transplant, Vol. 13, pp. 410-419. (1999).	
	CH6	Stratton et al., "Effects of Cardiac transplantation on Bioenergetic Abnormalities of Skeletal Muscle in Congestive Heart Failure." Circulation, Vol. 89, pp. 1624-1631. (1994).	

Examiner Signature		Date Considered
--------------------	--	-----------------

Substitute for form 1449/PTO				<i>Complete if Known</i>	
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Sheet	11	of	12	Attorney Docket Number	19240.596 US1

	CI6	Suisa, et al., "Bronchodilators and acute cardiac death," Am. J. Respir. Crit. Care Med. 154, 1598-1602 (1996).	
	CJ6	Suko et al., "Phosphorylation of Serine 2843 in Ryanodine Receptor-Calcium Release Channel of Skeletal Muscle by cAMP-, cGMP- and CaM-Dependent Protein Kinase." Bioch Biophys. Acta., Vol. 1175, pp. 193-206. (1993).	
	CK6	Sullivan et al., "Exercise Intolerance in Patients with Chronic Heart Failure." Prog. Cardiovasc. Dis., Vol. 38, No. 1, pp. 1-22. (1995).	
	CL6	Szabo et al. "Synthesis and Spectroscopic Investigation of 1,4-Benzothiazepine Derivatives." Magyar Kemiai Folyoirat, Vol. 93, No. 6, pp. 269-276. (1987). (in Hungarian and English)	
	CM6	Szabo et al. "Synthesis and Transformation of 4,5-dihydro-1,4-benzothiazepin-3(2H) - one derivatives." Magyar Kemiai Folyoirat, Vol. 93, No. 3, pp. 139-144. (1987). (in Hungarian and English).	
	CN6	Takeshima, H. et al. "Primary Structure and Expression from Complementary DNA of Skeletal Muscle Ryanodine Receptor." Nature, Vol. 339, pp. 439-445. (1989).	
	CO6	Tanabe, T. et al., "Regions of the Skeletal Muscle Dihydropyridine Receptor Critical for Excitation-Contraction Coupling." Nature, Vol. 346, pp. 567-569. (1990).	
	CP6	Tasken, et al., "Phosphodiesterase 4D and protein kinase a type li constitue a signaling unit in the centrosomal area," J. Biol. Chem. 276, 21999-2002 (2001).	
	CQ6	Timerman, Anthony P. et al., "The Calcium Release Channel of Sarcoplasmic Reticulum is Modulated by FK-506- binding Protein." J. Bio. Chem., Vol. 268, No. 31, pp.22992-22999. (1993).	
	CR6	Tse et al. "JTV-519 Japan Tobacco." Curr. Opin. Investig. Drugs. Vol. 2, No. 7, pp. 936-939. (2001).	
	CS6	Tsuji, N. et al., "Sudden Cardiac Death in Calves with Experimental Heavy Infection of Strongyloides Papillosus." J. Vet. Med. Sci., Vol. 54, No. 6, pp. 1137-1143. (1992).	
	CT6	Tunwell et al., "H. Sapiens mRNA for Ryanodine Receptor 2." GenBank Database, Accession No. X98330. September 9, 1996.	
	CU6	Tunwell et al., "The Human Cardiac Muscle Ryanodine Receptor-Calcium Release Channel: Identification, Primary Structure and Topological Analysis." Biochem. J., Vol. 318, pp. 477-487. (1996).	
	CV6	van Rooij, et al., "MCIP1 overexpression suppresses left ventricular remodeling and sustains cardiac function after myocardial infarction," Circ. Res. 94, e18-26 (2004).	
	CW6	Verde, et al., "Characterization of the cyclic nucleotide phosphodiesterase subtypes involved in the regulation of the L-type Ca ²⁺ current in rat ventricular myocytes," Br. J. Pharmacol. 127, 65-74 (1999).	
	CX6	Vest, J.A. et al., "Defective Cardiac Ryanodine Receptor Regulation During Atrial Fibrillation." Circulation. Vol. 111, No. 16, pp. 2025-2032. (2005).	
	CY6	Vignola, A.M., "PDE4 inhibitors in COPD--a more selective approach to treatment," Respir. Med. 98, 495-503 (2004).	
	CZ6	von Altrock, A., "Sudden Deaths in Fattening Herds on taking Blood Samples- Experiences from the Practice." Berl Munch Tierarztl Wschr, Vol. 112, pp. 86-90. (1999).	
	CA7	Wang, et al., "Cloning and characterization of novel PDE4D isoforms PDE4D6 and PDE4D7," Cell. Signal. 15, 883-891 (2003).	
	CB7	Wang, J. et al. "Physical Training Alters the Pathogenesis of Pacing-Induced Heart Failure Through Endothelium-Mediated Mechanisms in Awake Dogs." Circulation, Vol. 96, pp. 2683-2692. (1997).	
	CC7	Wehrens et al. "Ca ²⁺ /Calmodulin-Dependent Protein Kinase II Phosphorylation Regulates the	

Examiner Signature		Date Considered	
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		Cardiac Ryanodine Receptor." Circ. Res., Vol. 94, No. 6. pp. e61-70. (April 2004).	
	CD7	Wehrens et al., "Enhancing Calstabin Binding to Ryanodine Receptors Improves Cardiac and Skeletal Muscle Function in Heart Failure." PNAS, Vol. 102, No. 27, pp. 9607-9612. (2005).	
	CE7	Wehrens et al., "Molecular Determinants of Altered Contractility in Heart Failure." Ann Med., Vol. 36, Suppl. 1, pp. 70-80. (2004).	
	CF7	Wehrens et al., "Novel Therapeutic Approaches for Heart Failure by Normalizing Calcium Cycling." Nature Reviews Drug Discovery., Vol. 3, pp. 565-573. (2004).	
	CG7	Wehrens et al., "Protection from Cardiac Arrhythmia Through Ryanodine Receptor-Stabilizing Protein Calstabin2." Science, Vol. 304, pp. 292-296. (April 2004).	
	CH7	Wehrens et al., "Ryanodine Receptor-Targeted Anti-Arrhythmic Therapy." Ann N. Y Acad. Sci., Vol. 1047, pp. 366-375. (2005).	
	CI7	Wehrens et al., "Sudden Unexplained Death Caused by Cardiac Ryanodine Receptor (RyR2) Mutations." Mayo Clin Proc., Vol. 79, No. 11, pp. 1367-1371. (November 2004).	
	CJ7	Wehrens, et al., "Intracellular Calcium Release Channels and Cardiac Disease," Annu. Rev. Physiol. (2004).	
	CK7	Westphal, R.S. et al. "Regulation of NMDA Receptors by an Associated Phosphatase-Kinase Signaling Complex." Science, Vol. 285, pp. 93-96. (1999).	
	CL7	Wilson, et al. "Exertional Fatigue Due to Skeletal Muscle Dysfunction in Patients with Heart Failure." Circulation, Vol. 87, pp. 470-475. (1993).	
	CM7	Wilson, J.R. "Exercise Intolerance in Heart Failure. Importance of Skeletal Muscle." Circulation, Vol. 91, pp. 559-561. (1995).	
	CN7	Xiang, Y. et al.: "Phosphodiesterase 4D is required for β_2 adrenoceptor subtype-specific signaling in cardiac myocytes," PNAS, January 18, 2005, Vol. 102, no. 3, 909-914.	
	CO7	Xin, H.B. et al. "Oestrogen Protects FKBP12.6 Null Mice from Cardiac Hypertrophy." Nature, Vol. 416, pp. 334-337. (2002).	
	CP7	Yamamoto-Hino, M. et al. "Cloning and Characterization of Human Type 2 and Type 3 Inositol 1,4,5-trisphosphate Receptors." Receptor Channels, Vol. 2, pp. 9-22. (1994).	
	CQ7	Yamawaza, et. al., "Subtype Specificity of the Ryanodine Receptor for Ca^{2+} Signal Amplification in the Excitation-Contraction Coupling," The EMBO Journal, vol. 15, No. 22, pp. 6172-6177, 1996	
	CR7	Yang, Jiacheng et al. "A-kinase Anchoring Protein 100 (AKAP100) is Localized in Multiple Subcellular Compartments in the Adult Rat Heart." The Journal of Cell Biology, Vol. 142, No. 2, pp. 511-522 (July 27, 1998.)	
	CS7	Yano, M. et al. "FKBP12.6-Mediated Stabilization of Calcium-Release Channel (Ryanodine Receptor) as a Novel Therapeutic Strategy against Heart Failure." Circulation, Vol. 107, pp. 477-484. (2003).	
	CT7	Zaccolo, et al., "Discrete micro domains with high concentration of cAMP in stimulated rat neonatal cardiac myocytes," Science 295, 1711-5 (2002).	
	CU7	Zucchi et al., "The Sarcoplasmic Reticulum Ca^{2+} Channel/Ryanodine Receptor: Modulation by Endogenous Effectors, Drugs, and Disease States." Pharmacological Reviews, Vol. 49, No.1, pp. 1-51. (1997).	

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